Lecture Notes
Respiration

We will consider two processes by which organisms harvest energy from food molecules:

Aerobic Respiration—more efficient, occurs in presence of O_2
Anaerobic Respiration—less efficient, occurs in absence of O_2

Some organisms can survive using either kind of respiration (like yeast). Some rely principally on only one kind to survive. Humans, for example, rely on energy produced by aerobic respiration, and therefore require OXYGEN to survive. During strenuous exercise, oxygen becomes depleted in muscle tissue, and muscle cells can resort to a form of anaerobic respiration for a BRIEF period of time to meet demands—but the result is buildup of lactic acid, leading to muscle aches and fatigue.

We will begin with aerobic respiration:

Respiration = breathing. Thus it is the EXCHANGE of gases, O_2 for CO_2

However, cellular basis of breathing is the CHEMICAL PROCESS of **harvesting energy** from fuel molecules (including SUGARS). In this chemical process,

OXYGEN is CONSUMED
CARBON DIOXIDE generated as a WASTE PRODUCT.

This process occurs at CELLULAR level—so **cellular respiration.** Gas exchange occurs through blood circulation and lungs [see Figure 6.1]

Cellular respiration is Sugar + $O_2 \rightarrow$ **ENERGY** + CO_2 + H_2O

Note similarity here to process of **COMBUSTION**. Just like the energy to drive a car is generated by combustion of ENERGY RICH CARBON containing molecules (organic), the energy to operate all cells comes from combustion of energy rich carbon-containing fuel molecules.

We said earlier this semester that the "energy currency" of cells is **ATP**. (This is one of the nucleotides that are one of the bases in DNA!). THE OBJECTIVE OF CELLULAR RESPIRATION IS TO MAKE ATP.

So, for example, glucose ($C_6H_{12}O_6$) + 6 O_2 $\rightarrow$ 6 CO_2 + 6 H_2O + ATP

Note that the six carbon atoms in a glucose molecule are broken down into six carbon dioxide (CO_2) molecules to yield ATP. The reaction shown is greatly oversimplified. In reality, cellular respiration **disassembles** glucose (or other fuel molecules) in a **SERIES OF CHEMICAL REACTION STEPS**:

> Energy is "tapped" from electrons as they are rearranged in breaking old bonds and forming new ones.

Electrons start out in a molecule where they have more energy (**glucose**), and end up in a molecule where they have less energy (**water**), LIKE A BALL ROLLING DOWN A HILL. This energy is tapped at various

points during the downhill journey, and converted by proteins and enzymes into the useful form ATP. In between water and glucose are a number of **intermediate electron acceptors**, or **electron carriers**. .

Loss of electrons by one substance—**oxidation**
Gain of electrons by another substance--**reduction**

Respiration involves a series of electron-transfer reactions, as electrons "roll downhill" from higher to lower energy states. Since electron-transfer reactions require both an electron **donor** (the one that is "**oxidized**") and an electron **acceptor** (the one that is "**reduced"**), electron transfer reactions are called **oxidation-reduction reactions**, or **redox reactions**.

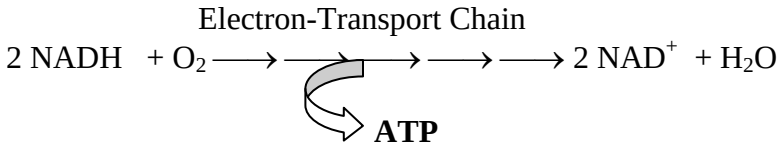
Notice in Figure 6.4 that the process of respiration also involves a transfer of hydrogen atoms. The overall result of respiration is the transfer of electrons, **along WITH hydrogen**, from a food molecule (like glucose) to oxygen, to produce water and ATP.

A key player in the transfer of electrons and hydrogen in the process of respiration is NAD^+ (from "nicotinamide adenine dinucleotide"). **NAD^+** is a "SHUTTLE" for carrying electrons and hydrogen, accepting electrons and hydrogen in the following reaction:

$$NAD^+ + 2H + 2e^- \rightarrow NADH + H^+$$

NADH is thus the REDUCED form of NAD^+. NADH molecules are generated at several different stages in the complex process of respiration, as we will see, and later "cashed in" for ATP, regenerating NAD^+. A single NADH molecule can be "cashed" in for as much as 3 ATP.

NADH delivers its "load" of high-energy electrons to an **electron-transport chain**, a SERIES of electron acceptors (most of which are specialized proteins). It is through the electron-transport chain that electrons "roll down" an energy hill. **The final electron-acceptor at the "bottom" of the hill is oxygen**. This is where oxygen is consumed in the process of respiration. NAD^+ is regenerated as NADH releases hydrogen as H^+. Hydrogen is picked up by oxygen to form water. Energy released in this process is used to produce ATP overall, the electron transport process can be described as:



The electron-transport chain is embedded in membranes in the **mitochondria**. The mitochondria are therefore the primary sites of ATP synthesis.

ATP is generated by **phosphorylation** reactions, in which a **high-energy** phosphate group is added to the lower energy precursor, ADP:

$$ADP + \textcircled{P} \longrightarrow ATP \text{ (high energy currency)}$$

ATP is actually generated by TWO mechanisms during the process of respiration.

Chemiosmotic Phosphorylation

This occurs as electrons journey through electron-transport chain. Most ATP in respiration is generated through this process. As electrons "fall" through the chain, some of the proteins in the chain actively "pump" hydrogen ions ("protons", H^+) across the inner mitochondrial membrane. This produces a higher concentration of H^+ in the intermembrane space than within the mitochondrial matrix. This represents a **concentration gradient** of H^+ ions that is a source of **potential energy** to drive the formation of ATP. In an attempt to equalize the H^+ concentration, H^+ ions flow through a special "channel" in the membrane, part of an enzyme called **ATP synthase,** which uses the energy of this H^+ **flow** to phosphorylate ADP and make ATP.

CELLS GENERATE MOST OF THEIR ATP THIS WAY

Substrate Level Phosphorylation

This occurs directly, as a phosphate group is **transferred** from an organic "substrate" molecule to ADP via a specific enzyme. This occurs at several steps during respiration, but does NOT involve the electron transport chain. Only a small amount of the total ATP produced by a cell is made this way.

<u>Overview of Respiration</u>

Three main stages [see Figure 6.8)

Glycolysis—occurs in CYTOPLASM. It involves breakdown of glucose from a six-carbon sugar into a 3-carbon compound called **pyruvic acid**. It produces a small amount of ATP by substrate-level phosphorylation, and a small amount of NADH.

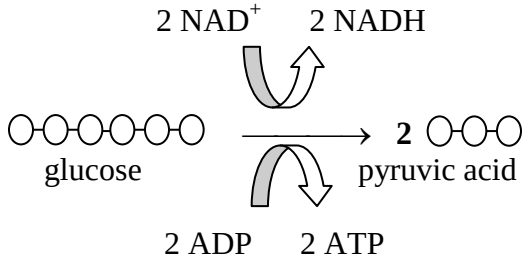
[NOTE: after glycolysis, pyruvic acid is "refined" into a compound called **acetyl coenzyme A**, before it can progress to the next stage, the "Krebs Cycle"]

Krebs Cycle—occurs in MITOCHONDRIA. Completes the breakdown of glucose by decomposing pyruvic acid into **carbon dioxide**. Produces a small amount of ATP, and much NADH (and $FADH_2$). Its main function is to provide high-energy electrons to the electron-transport chain.

The electron-transport chain—this is where most of the ATP is synthesized.

<u>Glycolysis in More Detail</u>

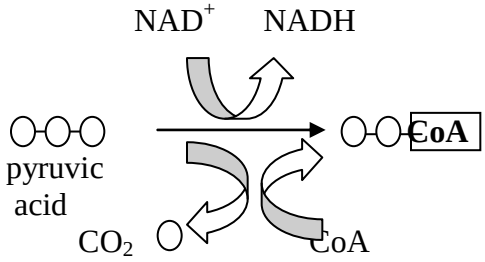
Glycolysis—literally means "splitting of sugar"—this is what literally happens during glycolysis. Glucose, a six-carbon sugar, is "split" into **TWO** 3-carbon pyruvic acid molecules. The result is 2 molecules of ATP are generated, plus two molecules of NADH which will be "cashed in" later for more ATP. The overall result is:



However, this picture is greatly oversimplified!! There are actually NINE steps to glycolysis, each catalyzed by a specific enzyme [you will NOT be responsible for knowing these nine steps, or the enzymes that catalyze them, but you WILL be responsible for knowing the overall reaction as diagrammed above].

Glycolysis only accounts for about 21% of the energy that a cell can ultimately harvest from a single glucose molecule. Most of the energy is released in the steps that follow.

Before pyruvic acid can progress to the next stage of respiration, it must be broken down and modified. In this process, a **single** carbon unit from pyruvic acid is lost as **carbon dioxide**, and a compound called "coenzyme A" is covalently attached (coenzyme A is derived from one of the B vitamins). The result is a **two-carbon** compound called **acetyl coenzyme A** (or **acetyl CoA**). Another molecule of **NADH is** generated in the process (or a total of TWO NADH per glucose molecule).



At this point, a single glucose molecule has been decomposed into **TWO** molecules of acetyl CoA.

Krebs Cycle in More Detail [see Figure 6.11]

The reactions of the Krebs Cycle occur in the **mitochondrial matrix.**

Coenzyme A is required only to help the **two**-carbon **acetyl** units enter the Krebs cycle. Once this has been accomplished, coenzyme A is stripped off. In the Krebs cycle, these two-carbon units are eventually broken down into **carbon dioxide**. In the process, a single molecule of ATP is generated (by SUBSTRATE--LEVEL phophorylation). Every acetyl unit that enters the cycle yields 1 ATP, 3 NADH, and one molecule of another electron and hydrogen carrier, $FADH_2$. The total energy output from the Krebs cycle for each molecule of glucose is 2 ATP, 6 NADH, 2 $FADH_2$. This is MUCH more than the amount of ATP and NADH yielded in glycolysis.

This picture is very oversimplified. Many steps are required, involving many intermediate compounds, and each step requiring a specific enzyme to catalyze it.

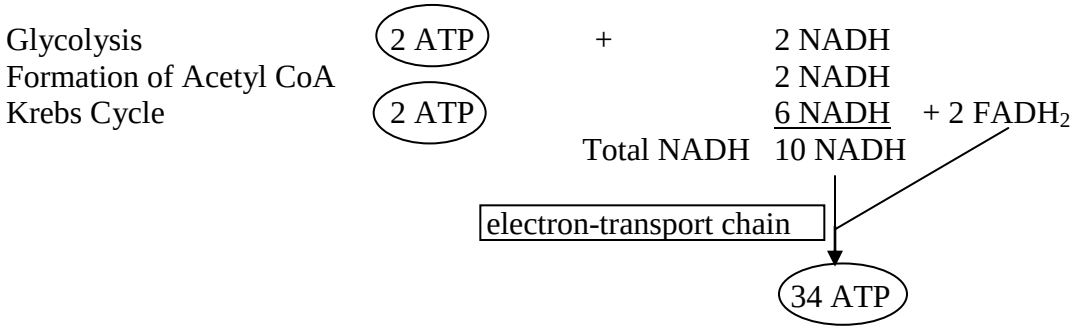
"Cashing in" NADH and $FADH_2$ for ATP in electron-transport chain

So far, a single molecule of glucose has yielded a very modest amount of ATP by substrate-level phosphorylation, a little bit of NADH from glycolysis and from conversion of pyruvic acid to acetyl-CoA, and LOTS of NADH (and $FADH_2$ from the Krebs cycle). It is now time to "cash in" the NADH and $FADH_2$ for ATP in the electron-transport chain. It is in the electron-transport chain that ATP is produced by **chemiosmosis** (remember--ATP in glycolysis and Krebs Cycle is produced by substrate-level phosphorylation). How much ATP does NADH and $FADH_2$ generate by delivering their load of electrons to the electron-transport machinery?

About **3** ATP per NADH
2 ATP per $FADH_2$

Summary of Aerobic Respiration

Let's look at the yield of ATP from the entire process of aerobic respiration now. The values given for each stage are for a single molecule of glucose.



Total ATP yield from aerobic respiration = 38 ATP
(however, 2 ATP are consumed in transporting the 2 NADH molecules produced during glycolysis from cytoplasm across mitochondrial membrane where they can be "cashed in" for ATP)

Fermentation—An Anaerobic Alternative to Aerobic Respiration

If oxygen is insufficient to support aerobic respiration, some organisms can harvest energy from fuel molecules by an alternative pathway, **anaerobic** ("without air") **respiration**. In anaerobic respiration, the 2 ATP produced during glycolysis is all that is harvested from a molecule of glucose—the Krebs Cycle and electron-transport chain are NOT utilized. Thus, anaerobic respiration is MUCH LESS EFFICIENT than aerobic respiration in using the potential energy contained in fuel molecules.

Furthermore, anaerobic respiration creates a problem—the pool of cellular NAD^+ is limited. In aerobic respiration, NAD^+ is regenerated after "unloading" its electrons and hydrogen atom into the electron-transport chain. In order to regenerate NAD^+ in the anaerobic type of respiration, an additional step is added:

In **yeast** and certain bacteria:

NAD^+ is regenerated by the conversion of pyruvic acid (product of glycolysis) into ethyl **alcohol**.
This is the basis of beer and winemaking.

In some kinds of cells (including human muscle):

NAD^+ is regenerated by the conversion of pyruvic acid into **lactic acid**.
This produces the sensation of sore muscles and fatigue. Eventually, lactic acid is carried away in the bloodstream and converted back to pyruvic acid in the liver.